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**Human neural stem cells differentiate and promote locomotor recovery in an early chronic spinal cord injury NOD-scid mouse model.**

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**Authors:** Desiree L Salazar, Nobuko Uchida, Frank P T Hamers, Brian J Cummings, Aileen J Anderson

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**Public Summary:**

**Scientific Abstract:**

**BACKGROUND:** Traumatic spinal cord injury (SCI) results in partial or complete paralysis and is characterized by a loss of neurons and oligodendrocytes, axonal injury, and demyelination/dysmyelination of spared axons. Approximately 1,250,000 individuals have chronic SCI in the U.S.; therefore treatment in the chronic stages is highly clinically relevant. Human neural stem cells (hCNS-SCNs) were prospectively isolated based on fluorescence-activated cell sorting for a CD133(+) and CD24(-/lo) population from fetal brain, grown as neurospheres, and lineage restricted to generate neurons, oligodendrocytes and astrocytes. hCNS-SCNs have recently been transplanted sub-acutely following spinal cord injury and found to promote improved locomotor recovery. We tested the ability of hCNS-SCNs transplanted 30 days post SCI to survive, differentiate, migrate, and promote improved locomotor recovery. **METHODS AND FINDINGS:** hCNS-SCNs were transplanted into immunodeficient NOD-scid mice 30 days post spinal cord contusion injury. hCNS-SCNs transplanted mice demonstrated significantly improved locomotor recovery compared to vehicle controls using open field locomotor testing and CatWalk gait analysis. Transplanted hCNS-SCNs exhibited long-term engraftment, migration, limited proliferation, and differentiation predominantly to oligodendrocytes and neurons. Astrocytic differentiation was rare and mice did not exhibit mechanical allodynia. Furthermore, differentiated hCNS-SCNs integrated with the host as demonstrated by co-localization of human cytoplasm with discrete staining for the paranodal marker contactin-associated protein. **CONCLUSIONS:** The results suggest that hCNS-SCNs are capable of surviving, differentiating, and promoting improved locomotor recovery when transplanted into an early chronic injury microenvironment. These data suggest that hCNS-SCNs transplantation has efficacy in an early chronic SCI setting and thus expands the "window of opportunity" for intervention.

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